material to promote poliovirus i-RNA transfection of HeLa cells was evaluated. Vehicle was 100 mM TES. 40%-positive effects. (Klebe, Hanson, Harriss & Bentley,1986).

Route: in vitro. Species: rat. A rat hepatocyte unscheduled DNA synthesis assay was conducted. [Data presented in Abstract form.]. 1 mg/ml-no effects. (Lee, Burger, Hayes & Doolittle,1988a).

Route: in vitro. Species: rat. The sample tested was spectranalyzed glycerol >99.5% pure. The autoradiographic unscheduled DNA synthesis assay (Mitchell & Mirsalis, 1984) was conducted using CD male rat hepatocytes. A positive result was a reproducible, dose-dependent increase in net nuclear grain counts compared to controls. No effects. (Doolittle, Lee & Lee,1988).

Route: in vitro. Species: rat. The ability of the test material to induce DNA damage in primary cultures of rat hepatocytes was investigated at 8 laboratories. Unscheduled DNA synthesis and DNA single-strand breaks were evaluated. No effects, at 10-100,000 ug/ml. (Fautz, Forster, Hechenberger, Hertner, vonderHude, Kaufmann, Madle, Madle, Miltenburger, et al.,1991).

Route: in vitro. Species: Saccharomyces cerevisiae. The ability of the test material to induce genetic change from [psi+] to [psi-] was evaluated. Vehicle was medium. The "well" test was used. 1800 millimolar-positive effects. (Tuite, Mundy & Cox,1981).

Teratogenesis and reproduction studies. Route: unclassified. Species: chick embryo. Test material was injected once per egg into the yolk sac or air chamber of White Leghorn eggs on different days of development. Mortality was evaluated throughout incubation. Gross

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morphology and skeletal changes were evaluated in survivors day 15. Materials were injected undiluted. 0.05 ml-reproductive effects, the maximum increased mortality was noted when injected into the air chamber on day 4 of incubation. Air chamber injections were made d 0-7. No effect was seen with yolk sac injection on day 4. (Gebhardt,1968).

Route: unclassified. Species: chick embryo. Toxicity and teratogenicity were evaluated under 4 conditions: injection via air cell or via the yolk sac at 2 times intervals (preincubation and 96 hr) for each route. Observations included mortality and structural & functional defects. Approximately 100 eggs per dose. Eggs from Single-Comb White Leghorn chickens were used. Dose listed is highest of 5 tested and units are actually mg/egg. Mortality is reported in the associated LD_{50} study. Vehicle was water. 75.00 mg-no effects. (Verrett, Scott, Reynaldo, Alterman & Thomas,1980).

Route: in vitro. Species: hydra. The assay method of Johnson et al.(1985) was used to determine the A/D ratio which was calculated as the adult minimal affective conc(MAC)/developmental MAC. Where possible, data were compared to, those of in vivo (Segment II-type) evaluations. Solvents used for specific chemicals were not indicated. Paper primarily summarizes current abilities and limitations of the assay as a prescreen for developmental toxicity. Unspecified effects, Hydra A/D = 1; Mammalian A/D not given. (Johnson, Newman, Gabel, Boerner, & Dansky,1988a).

Route: food. Species: rat. Select grps of young animals (strain unspecified) were maintained on diets containing test cpd. Experimental groups consisted of 3 M & 6 F animals. Pregnant females were removed

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from breeding cage & placed in individual cages before the litters arrived. Dietary treatment w/ test cpd remained the. Same during growth, reproduction & lactation. Young animals selected from the litter were continued on the same diet. At conclusion of ea. generation, representative adult animals were submitted to pathological examination. 30%-positive effects, animals receiving the glycerol diet were carried thru 7 generations successfully. (Guerrant, Whitlock, Wolff & Dutcher,1947).

Route: food. Species: rat. Fourteen groups of selected young animals (3 M & 6 F) were used. All animals were weighed @ weekly intervals and amt. of diet consumed measured. A special effort was made to formulate diets which retained optimal amts. of protein, minerals, vitamins, etc. after replacement of starch by isocaloric. Amts. of test cpd. When litters arrived, date, number of young born, and the average wt. of the young were recorded. Litters were weighed @ weekly intervals until they were weaned. Weaned females were weighed & mated. Mature M & F were subjected to pathological examination. 7.5%-reproductive effects, Glycerol fed females @ time of dropping of 1st litter were younger than propylene glycol-fed animals. 10%-reproductive effects, Glycerol-fed females @ time of dropping of 1st litter were younger than propylene glycol-fed animals. 20%-reproductive effects, Glycerol-fed females @ time of dropping of 1st litter were younger than propylene glycol-fed controls. 30%-reproductive effects, Glycerol-fed females @ time of dropping of 1st litter were younger than propylene glycol-fed controls. (Guerrant, Whitlock, Wolff & Dutcher,1947).

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Route: gavage. Species: rat. The Chernoff-Kavlock short-term in vivo assay (1982) for developmental toxicity was modified for use in the rat. Groups of 9-15 pregnant Alpk:AP (Wistar-derived) females received single doses (10ml/, kg) on Days 7-17 of gestation. Maternal BW on gestation Days 1, 7-12 & 22. Offspring observations were litter size & litter wt of live pups & no. of live & dead pups on Days 1 & 5 postpartum. Results compared to conventional teratology tests. Vehicle not specified. There were no false positives. 600 mg/kg-reproductive effects, reduced litter size, neonatal survival & BW gain. Predicted to be a teratogen. (Found to be teratogenic when given by IP & SC routes in conventional tests.) (deWickramaratne,1987).

Route: oral. Species: rat. Fifty-one animals/dose grp were fed varying quantities of a standard diet in which starch was replaced by equal wts. of test cpd for 40 wks. An evaluation of reproductive activity was also made. The number of pregnancies, young born & young weaned were observed. [No further experimental detail. Given]. 41%-no effects. 61%-reproductive effects, no pregnancies occurred. Paper states this "is to be expected from the undernourished & debilitated condition of the animals.". (Johnson, Carlson & Johnson,1933).

Route: skin. Species: rat. The sample tested was present in formulation @ 4.5%. As a continuation of protocol 01, after the first F1a litters had been weaned the number of F0 parents was reduced from 40 to 20 animals in ea. grp. After a 10-day rest period the remaining animals were re-mated to produce the F1b litters. Pups were counted & weighed as a litter on days 0, 4, & 14. Of lactation. On day 21 of lactation pups were counted, sexed, weighed individually & observed for

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signs of pharmacological effects. Indices for live birth & survival to weaning were then calculated. Irritant effects, the principal difference between the controls & groups treated w/ formulations was skin irritation (mild dermatitis) seen intermittently throughout the treatment period. (Burnett & Goldenthal,1988a).

Route: skin. Species: rat. The sample tested was present in formulation @ 4.5%. Twenty male & 20 female Sprague-Dawley animals/grp were selected from the F1b litters (see Protocol 02) to become F1 parents of the next generation. Animals were selected from all litters & test cpd applied topically for 100 days. After 100 days, animals were mated, to produce F2a & F2b litters. After F2b litters had been weaned, five male & five female F1 animals were necropsied & tissues taken for histopathological exam. Irritant effects, the principal difference between the controls & groups treated w/ formulations was skin irritation (mild dermatitis) seen intermittently throughout the treatment period. (Burnett & Goldenthal,1988a).

Route: skin. Species: rat. The sample tested was present in formulation @ 4.5%. Three hundred and sixty Sprague-Dawley animals were assigned to nine grps of 40 animals ea. Test cpds were topically applied to animals until they were 100 days old. Animals were paired & mated. Pups delivered were counted & weighed as a litter on days 0, 4, & 14 of lactation. On day 21 of. Lactation pups were counted, sexed, weighed individually & observed for signs of pharmacological effects. Indices for live birth & survival to weaning were then calculated. Irritant effects, the principal difference between the controls & groups treated w/ formulations was skin irritation (mild dermatitis)

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seen intermittently throughout the treatment period. (Burnett & Goldenthal,1988a).

Route: unclassified. Species: monkey. 10 male Bolivian or Guyanan squirrel monkeys received an intratesticular injection of test material. Vehicle was water and ethanol. Blood and semen samples were collected throughout the study. Reproductive tissues were collected at the 22 month termination from 3 control and 7 treated monkeys. Parameters evaluated included body weights, organ weights, serum hormone levels, sperm counts and testicular steroidogenesis measurements. 50%-reproductive effects, Sperm count declined to near zero within 2 months and remained at zero. Testes and epididymides weights were decreased. Serum LH increased months 6 and 7. FSH levels increased months 6-8. (Wiebe, Barr & Buckingham,1989).

Route: unclassified. Species: rat. Young adult male Sprague-Dawley animals were anesthetized, and scrotum inj w/ test cpd or saline. At 1, 2, 8 or 36 wks following injection, 6-10 control and 6-10 treated animals were weighed, sacrificed and testes, accessory sex organs and serum analyzed as to weight, function and hormonal levels. 10%-organ weight changes, reproductive effects, sign. reduction in gonad wt. noted. Total number of sperm in epididymes sign. reduced. 20%-organ weight changes, reproductive effects, sign. reduction in gonad wt. noted. Total number of sperm in epididymes sign. reduced. 40%-organ weight changes, reproductive effects, sign. reduction in gonad wt. noted. Total number of sperm in epididymes sign. reduced. 70%-organ weight changes, reproductive effects, sign. reduction in gonad wt. noted. Total number of sperm in epididymes sign. reduced. (Igdoura &

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Wiebe,1994).

Route: unclassified. Species: rat. Male Sprague-Dawley animals, aged 60-75 years were lightly anesthetized w/ ether, scrotum was wiped w/ alcohol, and control or test cpd sol'n was injected into ea. testis. Control animals received saline, whereas the treated group received saline containing test cpd. Treated or control animals (n= 5-15) under light ether anesthesia also received an intratesticular inj of [3H]inulin. One hour after inj., animals were sacrificed and testes were removed, weighed, decapsulated. Tissue was gently teased apart, washed in buffer, digested and accumulated radioactivity measured. 20%-positive effects, a 2.9-fold greater accumulation of radioactivity than in control testes noted. (Eng, Wiebe & Alima,1994).

Route: unclassified. Species: rat. Eighty young adult male Sprague-Dawley animals were anesthetized and scrotum inj. w/ test cpd or distilled water. At 1,2,4, or 8 wks following inj, 10 control & 10 treated animals were sacrificed. Weight of testes & epididymides, as well as epididymal sperm number, were determined. In addition, testicular histology was evaluated. Serum. conc. of follicle-stimulating hormone (LH), testosterone, & antisperm antibody and testicular FSH & LH receptor content were determined. 10%-organ weight changes, reproductive effects, sign. reduction of spermatozoan stored in epididymides noted. Gradual loss of all types of germ cells in the majority of seminiferous tubules also observed. (Igdoura & Wiebe,1994).

Route: unclassified. Species: rat. Twenty young adult male Sprague-Dawley animals were anesthetized and scrotum inj. w/ test cpd.

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At 2 and 6 weeks following inj; 5 untreated & 5 treated animals were sacrificed and testes removed & detunicated. Each testis was homogenized in buffer & centrifuged. Supernatant was used immediately for GTP activity or was stored frozen for 2 days @ 20 C before measuring LDH activity. 10%-enzyme inhibition, enzyme induction, 50% reduction in LDH (germ cell enzyme) activity on a per-testis basis and a 58.2% increase in GTP activity after the 8th wk noted. (Igdoura & Wiebe,1994).

Route: unclassified. Species: rat. In order to compare the effects of intratesticular inj of equiosmolar soln's of test cpd on testicular histology, 30 90 day old male Sprague-Dawley animals were divided into three grps and inj. w/ test cpd or distilled water. Animals were sacrificed @ 4 wks after the injection. Wts of testes, Epididymides, prostate gland, and seminal vesicles as well as epididymal sperm number, serum conc. of follicle-stimulating hormone, luteinizing hormone, and testosterone, and testicular histology were determined. 10%-organ weight changes, reproductive effects, 34% reduction in testicular wt. & a 32% reduction in epididymal wt noted. Epididymal sperm numbers were sign. reduced in both treatments. Glycerol more effective in suppressing spermatogenesis. (Igdoura & Wiebe,1994).

Route: unclassified. Species: rat. Male Sprague-Dawley animals, aged 60-75 days, were anesthetized, scrotum wiped with alcohol, and control or test cpd inj into ea. testis. Four wks following treatment of 8 animals, testes, epididymides were removed as a unit. To prevent leakage of fluid, epididymides were ligated 1.5 cm from. The caput region. [3H]inulin was administered intratesticularly. Tissues were

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incubated for 1 hr @ 34 C. Following incubation, testes were decapsulated, gently teased apart, washed in buffer, digested overnight, and accumulated radioactivity determined. 20%-positive effects, [3H]inulin accumulation in treated tissues was about 10-fold greater than in controls. (Eng, Wiebe & Alima,1994).

Route: unclassified. Species: rat. Male Sprague-Dawley animals, aged 60-75 days, were anesthetized, scrotum wiped with alcohol, and control or test cpd inj into ea. testis. Four wks following treatment of 8 animals, testes were removed and decapsulated. Some decapsulated testes were gently teased, taking care not to rupture the. Tubule segments (about 2 cm in length; 80 mg total) which were isolated. Tissues were then incubated for 1 hour @ 34 C in a sol'n containing [3H]inulin. Following incubation, tissues were washed in buffer, digested overnight and then accumulated radioactivty determined. 20%-positive effects, seminiferous tubule fragments isolated from glycerol-treated teste 4 wks after treatment showed 9.9-fold greater accumulation of [3H]inulin than those from control testes. (Eng, Wiebe & Alima,1994).

Route: unclassified. Species: rat. Male Sprague-Dawley animals, aged 60-75 days, were anesthetized, scrotum wiped with alcohol, & control or test cpd inj into ea. testis. Two, 4, 8, 26 & 56 wks after treatment, animals were anesthetized, testes were exposed through an abdominal incision, & efferent ducts were ligated w/ silk thread. Testes were returned to scrotum, wound was cleansed & closed & animal was allowed to recover. Six to 8 hrs after afferent duct ligation, animals were lightly anesthetized w/ ether, scrotum was wiped with

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alcohol & [3H]inulin was inj. intratesticularly. Rete fluid collected; radioactivity measured. Positive effects, radioactivity in the rete testis fluid of treated testis was 5.5-, 9.4-, 4.1-, 11.1-, and 22.4-fold greater @ 2,4,8,26 & 56 wks, resp. than in controls. (Eng, Wiebe & Alima,1994).

Route: in vitro. Species: pig. Embryos were surgically collected from 4 anesthetized Yorkshire gilts on days 5.5 to 7.5 of the estrous cycle. A total of 182 embryos ranging in developmental stage from compact morula to hatched blastocyst was obtained from 16 naturally cycling donors. Embryos were placed in test cpd @ room temp. For 30 sec, and transferred to 1.0 M sucrose for 20 min @ 39 C, followed by transfer to 39 C holding medium for 15 min @ which time they were evaluated. Embryos were cultured for 48 hrs & evaluated. 10%-no effects. 20%-positive effects, 78% of the embryos continued morphologic development. 30%-positive effects, 75% of the embryos continued morphologic development. 40%-positive effects, 6% of the embryos continued morphologic development. 50%-positive effects, 0% of the embryos continued morphologic development. (Weber & Youngs,1994).

Route: in vitro. Species: rat. The whole embryo culture method was used with embryos of Wistar rats segregated according to their precise stage of development. A 4 hour incubation with test material in serum was conducted. The embryos were assessed for growth and development. Additional tests were conducted with distilled water added to the test material-serum mixture in order to correct the osmolality created by the test material. Reproductive effects, embryos grown in serum with glycerol and distilled water grew better than those in glycerol alone

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although slight growth defects and some abnormal development persisted. (Clode, Pratten & Beck,1987).

Neurotoxicity. Route: intraperitoneal. Species: mouse. Solvents diluted with H2O & given in increasing doses at 10ml/kg (20ml/kg for high doses) to groups of 3 NMRI males (18-22g). Performance of the CNS-profile test & classification of solvents were, made by the criteria of Campbell & Richter (1967) 30 minutes later. , min. symptomatic dose=6.0g/kg. Piloerection & convulsions observed ante mortem. No classification. (Budden, Kuhl & Bahlsen,1979).

Route: intraperitoneal. Species: mouse. Solvents diluted with H2O & given in increasing doses at 10ml/kg (20ml/kg for high doses) to groups of 3 NMRI males (18-22g). The inclined screen test was performed. Mice not climbing up within 5, minutes were regarded as reactors. ED50 values calculated by method of Behrens & Karber (1935). , ED50>5.0 g/kg. (Budden, Kuhl & Bahlsen,1979).

Route: intraperitoneal. Species: mouse. Solvents diluted with H2O & given in increasing doses at 10ml/kg (20ml/kg for high doses) to groups of 3 NMRI males (18-22g). The balance rod (metal bar 40cm x 8mm) test was performed 30-35 min later. Mice that dropped off or didn't run were regarded as reactors. ED50 values calculated by method of Behrens & Karber (1935). , ED50 approximately 5.0 g/kg. (Budden, Kuhl & Bahlsen,1979).

Route: oral. Species: mouse. Mice were trained to run on a rotating rod. Solvents diluted with H2O & given in increasing doses at 10ml/kg to groups of 4 NMRI males (18-22g). Time until dropping off (max 60 sec) was then, determined 40, 60, 90 & 135 minutes

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postinjection. , min. dose producing drop off = 0.3g/kg. (Budden, Kuhl & Bahlsen,1979).

Route: oral. Species: mouse. Solvents (6.25 - 100% aqueous soln) were given at 10ml/kg to groups of 6 NMRI females (18-22g). Sixty min later, mice received hexobarbitone at 64mg/kg, IV & sleeping times until return of righting, reflex were measured. ED50a(1:2)- or ED50b(1:4)-potentiation of sleeping time in 1/2 of the mice- was calculated by probit analysis. , ED50a = 3.6 (2.45 - 5.18) g/kg; ED05a = 0.78g/kg. (Budden, Kuhl & Bahlsen,1979).

Route: intragastric. Species: rat. Several experiments were conducted using male Sprague-Dawley rats. Observations included food & water intake, urinary output, equilibrium & voluntary activity level. Test material was given neat or with corn oil or water. Isocaloric and isovolumetric controls were included as needed. Each rat received a single dose of each test material and control with a different material (or dose) given each day, 5 days a week for up to 3 weeks. The rats were restrained for some experiments and appropiately trained for others. Holtzman and Long-Evans rats were used for some experiments. Positive effects, dose-related decreases were seen in food intake and voluntary activity with an increase in water intake at doses of 2.5-10.5 g/kg. (Ayres & Isgrig,1970).

Cytotoxicity. Route: in vitro. Species: chicken. Fertile hen eggs were maintained at constant temp. and humidity. On day 4 of development, 2.5 ml of albumin was removed through pointed end of eggs using a needle and syringe. A wheel bit on a dental drill was used to cut a rectangular window in side of the shell over position of the

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embryo. The. Hole was covered with transparent tape. On day 14, window tape was peeled back, a Teflon ring placed on the CAM and 40 ul of test material pipetted onto CAM. Window was resealed with tape and eggs incubated until day 17. CAMs were then examined for lesions and lesion dimensions measured. 100%-positive effects, CAMVA RC50 value was 12%. (Bagley, Booman, Bruner, Casterton, Demetrulias, Heinze, Innis, McCormick III, Neun et al,1994).

Route: in vitro. Species: adult human. A human hepatoma cell line was used with a 24 hour incubation at 37°C. A range of concentrations was tested in triplicate for each test material. Vehicle not given. This test was conducted to evaluated its potential as an alternative to the Draize rabbit eye irritation test. 0.7%-no effects, highest tolerated concentration (98 mM) (Stark, Shopis, Borenfreund & Walberg,1983).

Route: in vitro. Species: adult human. The cultured corneal endothelial cell model system was used. Cell viability was measured via the 51Cr release assay. Vehicle not given. , ED50=25 M (99 M to 7.9 M) (Douglas & Spilman,1983).

Route: in vitro. Species: adult human. Human keratinocytes harvested after enzymatic detachment were used as 3-dimensional cell aggregates or as adherent multilayers in microtiter plates to evaluate irritancy potential of 13 chemicals: surfactants, alcohols, aldehydes & ketones. Determined neutral red uptake (measure of lysosomal, integrity or cell viability) & MTT reduction (measure of mitochondrial activity or cell metabolism) by incubating keratinocytes for 24 hr with various conc of chemicals using 8 wells/conc. Compared data to both in

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vivo toxicity data & in vitro 3T3 data. NR50=conc causing 50% decrease in absorption. , keratinocyte sheets NR50 = 200 mg/ml; 3T3 fibroblast NR50 = 71 mg/ml; in vivo = nonirritant (eye & skin). (Hoh, Maier & Dreher,1987).

Route: in vitro. Species: adult human. Living dermal equivalents were constructed from human dermal fibroblasts isolated from neonatal foreskins and acellular collagen. Polyethylene rings were affixed to upper surface of living dermal equivalent and test samples were applied to center of washers. Exposed LDE were incubated for desired times (1 min - 24 hr). At end of exposure period, upper surface of LDE was rinsed to remove any traces of test sample & set in medium containing MTT & incubated for 3-4 hr @ 37 C. At end of staining period, exposed portion of LDE was excised, extracted & MTT conversion measured. 100%-positive effects, EC50 value was greater than 70. (Bagley, Booman, Bruner, Casterton, Demetrulias, Heinze, Innis, McCormick III, Neun et al,1994).

Route: in vitro. Species: mouse. Uridine uptake assay using Balb/c 3T3 fibroblast cells and a 4 hour incubation. Vehicle was growth medium. The UI50 is that dose which inhibits 50% of the uridine uptake of untreated cells. UI50 results of this test have been found to correlate well with the relative irritancies of the test substances as reported in published Draize rabbit eye irritation tests. 6%-positive effects, UI50. (Stark, Shopis, Borenfreund & Walberg,1983).

Route: in vitro. Species: mouse. Inhibition of the rate of uptake of [3H]uridine by cultured BALB/c 3T3 cells was measured after a 4 hour incubation in test medium. The UI50 is that concentration which

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inhibits uptake by 50%. Rankings based on the UI50 values were found to correlate well with published data on Draize rabbit eye tests. Additional tests on mixtures indicated that the effects of combinations of agents are greater than those of the individual components. Some data is the same as that published in Shopsis84. Positive effects, UI50>800 mM. (Shopsis & Sathe,1984a).

Route: in vitro. Species: mouse. The A31-1-13 clone of BALB/C-3T3 cells was used to study chemically-induced transformation in a standard transformation assay protocol. Each transformation assay contained three components: a standard clonal survival assay, a co-culture clonal survival assay and a. Transformation assay. Chemically-induced transformation was detected in 18-20 vessels/dose seeded w/ 3.24 X 10(4) cells/vessel. Chemical doses were applied to cell cultures for 48 hr; days 2-4, using standard procedures. 401 millimolar-calculated LD_{50}, positive effects, Transformation responses from 2 trials graded as "sufficient positive". (Matthews, Spalding & Tennant,1993a).

Route: in vitro. Species: rat. Male Wistar animals were adm. test subst. in diet or drinking water & sacrificed after certain periods of time, ranging from 1 wk to 3 mo. A total of 15 animals were used for ea. of the test subst & 3-4 animals were sacr. @ ea. time period. Control animals received powdered complete diet. A part of the liver from sacrificed animals was cut into small pieces, & fixed for electron microscopic analysis. diluted v/v in water. 30%-liver, remarkably enlarged mitochondria in all hepatocytes were noted after one month exposure. (Wakabayashi, Adachi & Popinigis,1991).

Route: in vitro. Species: rabbit. The sample tested was Vehicle

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was 50% ethanol in buffered saline. Test material was incubated with primary rabbit cornea cells for 20 min. The cells were obtained from a Japanese white rabbit. The LD_{50} is the dose which gives 50% survival of the cells. The LD37 is the dose which gives 37% survival of the cells. 0.035%-calculated LD_{50}, LD37 = 0.055%. (Watanabe, Watanabe, Suzuki, Nikaido, Ishii, Konishi, Tanaka & Sugahara,1989a).

Route: in vitro. Species: rabbit. Cultured corneal epithelial cells were exposed to test sol'n for 5 min following removal of culture medium and rinsing. After removal of test cpd, cells were rinsed serum-free and medium added. Cells were maintained for 2-day recovery period during which the culture medium was collected for assay. Of plasminogen activator (PA). Plasminogen activation was assayed photometrically. 100%-positive effects, CEPA score was 249. (Bagley, Booman, Bruner, Casterton, Demetrulias, Heinze, Innis, McCormick III, Neun et al,1994).

Enzyme induction. Route: in vitro. Species: rat. Cytochrome c oxidase was added to a reaction cell containing buffer, test cpd & ferrocytochrome C derived from horse heart. Initial velocities of reaction of cytochrome c oxidase-catalyzed aerobic oxidation of ferrocytochrome C were measured spectrophotometrically in the presence of test cpd. Kinetic constants were determined. , pKi value was -0.03 M. (Value taken from graph). (Hasinoff & Davey,1989).

Route: in vitro. Species: rat. The effect of test material on the release of B-hexosaminidase by rat basophilic leukemia cells (RBL-2H3) was studied. Doses were in the range of 1-1000 uM. The enzyme ativity of B-hexosaminidase was measured as an index of chemical mediator

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release. Promotion of this release is triggered by cell injury. Vehicle was water. No effects. (Tanaka, Takagaki & Nishimune,1991).

Miscellaneous. Route: surface of eye. Species: rabbit. Aqueous humor concentrations were determined after a single application of test material to the corneas of male albino rabbits. Vehicle was isotonic Sorensin's buffer. , increased viscosity of the vehicle had no effect on the penetration rate of glycerol. (Grass & Robinson,1984).

Route: intravenous. Species: cat. Twenty-two animals weighing 2.5 to 3.5 kg were used. Pentobarbital was used for intravenous anesthesia. A tracheostomy was performed & ventilation monitored w/ respirator. Arterial blood gas levels were monitored regularly & maintained @ physiologic levels. Perilymphatic pressure, cerebrospinal. Fluid pressure, central venous & arterial presure were measured. The cochlear aqueduct (CA) was blocked via the tympanic bulla in 14 animals. Five animals received test cpd before obstruction of the CA & 2 of these received test cpd 4 hrs after blocking the CA. Arterial blood samples were drawn. 1.2 g/kg-positive effects, equal reduction of the cerebrospinal fluid & perilymphatic pressure was noted upon exposure to test cpd. (Carlborg & Farmer Jr.,1983).

Route: intravenous. Species: adult human. Thirty-six pts w/ 37 acute cerebral infarctions were treated w/ test cpd between July 1970 & May, 1971. The diagnosis was based on sudden onset of severe, persistent neurological deficit lasting 48 h(34 pt) or 72 h (2 pts). Test cpd was adm as a 10% sol'n in saline or dextrose & water @ a dosage of 1.2 g/kg body weight every 24 h. Treatment was started w/in 72 h of the onset of cerebral infarction. 1.2 g/kg-positive effects, of

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the 9 patients dosed iv, 8 were classified as improved @ the final outcome of the study. (Meyer, Charney, Rivera & Mathew,1971).

Route: intravenous. Species: adult human. Seventeen patients w/ edema of the central nervous system were given test cpd[dose not specified]. Six had cerebral anoxia due to cardiac arrest or ventricular fibrillation, eleven had various other types of edema of the central nervous system. Neurological status was determined daily & improvement was recorded if there were signs of increased strength in the paralysed extremity or extremities or improvement in the mental status or both. Positive effects, of the 8 patients given glycerol iv, 3 were classified as improved or symptom-free as a final outcome. (Meyer, Charney, Rivera & Mathew,1971).

Route: intravenous. Species: adult human. A 55-yr old male w/ a history of moderately raised blood pressure was found unconscious during his afternoon nap. A stroke was diagnosed because of tetraplegia and palsy of soft palate. 40 mg frusemide & 0.25 mg K strophantoside were given intravenously. Intravenous infusion of test cpd was begun. Three and one-half hr after admission and it lasted about 20 min. Effects on pt. noted. 10%-neurological effects, kidney, birefringent cyrstals were noted occasionallly in the medial layer of the meningeal & intracerebral arteries. A mass of similar crystals was seen in the lumina of renal tubules. (Krausz, Sellyei & Abranyi,1977).

Route: intravenous. Species: adult human. Eighteen subjects (10 males & 8 females, aged 52-82) hospitalized within a few hours from onset of symptoms for an ischemia or hemorrhagic acute stroke were

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studied. Soon after admission, all pts were treated w/ 60 min continuous adm. of test cpd in 500 ml of isotonic saline. The adm. was repeated. Every 24 hrs for the following 2 days. In addition, according to the therapeutic scheme, ea. pt. received 8 mg of dexamethasone (DECADRON), iv twice daily & were allowed to drink only water or light tea for the first 3 days of treatment. Hemorheologic parameters were evaluated on blood samples. 500 ml-blood effects, whole blood viscosity was significantly lower than mean basal value after 2 & 6 hrs. Plasma viscosity showed a constant decrease from the basal value. Decrease became statistically sign. after 6 hrs. (Tonelli, Catamo, Molina, Mombelloni, Ponari, Squeri & Tardio,1990).

Route: intravenous. Species: infant under 1 year. The patient, was a full-term 7 lb, female product of a spontaneous vaginal delivery. At 1 day of age, hyperpnea & lethargy were noted and laboratory studies revealed a severe metabolic acidosis. Integrity of the gluconeogenic enzyme system was examined by determining the glycemic responses of pt. Intravenous infusions given over 5 min of soln's of test cpd given 6 & 12 hr postprandially. Blood samples were obtained from an indwelling needle in the brachial vein. Positive effects, caused a rapid fall in plasma glucose and a concomitant increase in blood lactate, 2-3 mM above baseline levels. (Pagliara, Karl, Keating, Brown & Kipnis,1972).

Route: intravenous. Species: infant under 1 year. After an overnight fast, an open liver biopsy was performed on subject. Liver slices were prepared w/in 10 min after obtaining the biopsy. Two to three slices w/ a total wet wt. of 50 mg were distributed into 25 ml

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Erlenmeyer flasks containing Krebs-Ringer bicarbonate, w/ & w/o test cpd. Incubations were performed in duplicate for 90 min @ 37 C and medium was assayed for glucose, lactate, & pyruvate content. Positive effects, 75% increase over controls in lactate production noted. (Pagliara, Karl, Keating, Brown & Kipnis,1972).

Route: oral. Species: 1-13 year old child. A 3-yr old Caucasian boy was referred for evaluation of "hypoglycemia". One morning, @ 11 month of age, he was found to be pale, sweating and unrousable with ketonuria and a blood glucose concentration of 29 mg/dl following a gastrointestinal upset the previous day. Metabolic studies were performed. After an overnight fast which followed 48 hr of normal food uptake. Test cpd was adm. in water. 0.5 g/kg-positive effects, after a 9 hr fast, oral glycerol provoked euphoria, confusion, drowsiness, nausea, vomiting, & diarrhea. 2.5 to 3 hr after ingestion. 1.0 g/kg-positive effects, after a 10 hr fast, rapid fall in blood glucose concentration from 93 to 35 mg/dl within 60 min, accompanied by a fall in plasma phosphate, a slight fall in lactate, and an elevation in alanine concentrations were noted. (Maclaren, Cowles, Ozand, Shuttee & Cornblath,1975).

Route: oral. Species: domestic animals. No results in computer files. (Sauer, Erfle & Fisher,1973a).

Route: oral. Species: adult human. Seventeen patients w/ edema of the cental nervous system were given test cpd[dose not specified]. Six had cerebral anoxia due to cardiac arrest or ventricular fibrillation, eleven had various other types of edema of the central nervous system. Neurological status was determined daily & improvement was recorded if

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there were signs of increased strength in the paralysed extremity or extremities or improvement in the mental status or both. Positive effects, of the 9 patients given glycerol orally, 3 were classified as improved or symptom-free as a final outcome. (Meyer, Charney, Rivera & Mathew,1971).

Route: oral. Species: adult human. Thirty-six pts w/ 37 acute cerebral infarctions were treated w/ test cpd between July 1970 & May, 1971. The diagnosis was based on sudden onset of severe, persistent neurological deficit lasting 48 h(34 pt) or 72 h (2 pts). Test cpd was adm as a 10% sol'n in saline or dextrose & water @ a dosage of six divided doses of 1.5 g/kg every 24 h. Treatment was started w/in 72 h of the onset of cerebral infarction. given in orange or lemon juice. 1.5 g/kg-positive effects, of the 27 patients dosed orally, 21 were classified as improved @ the final outcome of the study. (Meyer, Charney, Rivera & Mathew,1971).

Route: oral. Species: adult human. A 68-year-old woman sustained renal failure after ingestion of test cpd. Exsiccosis which followed the test cpd ingestion led probably to the terminal renal failure. [Article in German; summary in English]. Kidney, terminal renal failure noted. (Ranner, Dirnhofer & Maurer,1986).

Route: oral. Species: mouse. The sample tested was in drinking H2O. Examined whether 5% glycerol in the drinking H2O would cause abnormal cell proliferation in the lungs. An Alzet minipump filled with 1 mCi [3H]methylthymidine was implanted under the skin of the backs of A/J mice at the beginning of exposure to glycerol & at the beginning of the 4th, 7th & 10th wks. Mice sac'd 3 wks after

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implantation & lung tissue prepared for autoradiography. Cumulative labeling indices were determined in parenchyma & small airways. 5%-no effects, on cell proliferation in the alveolar zone or in the small airways. (Witschi, Malkinson, Peraino, Russell & Staffeldt,1989).

Route: subcutaneous. Species: dog. Eight animals were inj. w/ test cpd 14 times (time period unspecified). [No further experimental detail given]. 2.5 g/kg-kidney, albuminuria occurred twice & hemoglobinuria 3 times. Injections were 2.5 to 3.0 gm/kg. (Johnson, Carlson & Johnson,1933).

Route: skin. Species: adult human. No results in computer files. (Leveque, Corcuff, Gonnord, Montastier, Renault, Bazin, Pierard & Poelman,1995).

Route: unclassified. Corbicula, the Asiatic clam, was used as an indicator species in studying the effect of chloroorganic discharges from power plants. Qualitative analysis was conducted on clam and water samples. Analysis was done on samples taken near power plants. Materials in the results section were found in specific samples as indicated in their notes as follows: CW=control water samples; TW=treated water samples taken after release of chloroorganics; CC=control clam samples; TC=treated clam samples. Positive effects, present in CW, CC and TC samples. (Lee, Haag, & Jolley,1981).

Route: unclassified. Species: rabbit. The ability of the test material to reversibly or irreversibly damage the blood-brain barrier was evaluated. Intravascular Evans Blue-albumin complex was used to evaluate permeability of barrier. A circular filter paper pladget was placed on the cortical region & saturated w/test material for 10 min.

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Anesthetized rabbits were used. Vehicle was water. , the threshold for blood-brain barrier opening was 5.0 molal. The opening was reversible. (Rapoport, Hori & Klatzo,1971).

Route: unreported. A rotating diffusion cell was used to measure diffusion. A filter was impregnanted w/ a test cpd, aqueous phase was added to the outer compartment and both compartments were then filled simultaneously. Transport process was followed by using the pH stat technique or by removing samples every hour or so & measuring the conc. spectrophotometrically. Viscosities were determined using Ostwald viscometer. Diffusion coefficients were measured using a Stokes cell. Partition coefficients were determined by shaking the system for @least 24 hr & analyzing for substrate spectrophotometrically/pH stat. 60%, the partition coefficient K was approx. 1 when methyl nicotinate was present as substrate, isopropyl myristate in filter and water/glycerol mix in inner phase. 80%, the partition coefficient K was approx. 1 when methyl nicotinate was present as substrate, isopropyl myristate in filter and water/glycerol mix in inner phase. (Albery, Burke, Leffler & Hadgraft,1976).

Route: in vitro. Species: fungi. The onset of inhibitory action of test cpd(s) upon cell multiplication of the blue-green alga, Microcystis aeruginosa and the green alga, Scenedesmus quadricauda was determined and the test cpd concentration causing the onset of cell multiplication inhibition in ea. case (toxicity threshold = TT) for both test organisms established. On this basis the ratio between toxicity threshold of ea. tested substance for the blue-green alga (TTmi) and the toxicity threshold of the corresponding substance for

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the green alga (TTsc) was calculated by setting TTmi = 1. , TTmi = 2900 mg/l; TTsc >10000 mg/l. (Bringmann & Kuhn,1978).

Route: in vitro. Species: guinea pig. The effect of immersion in test material on the penetration of light through stratum corneum was evaluated. The spectral transmission curve for isolated stratum corneum was measured under ambient conditions and after complete immersion of the stratum corneum in neat test material. The wavelengths measured were 320 and 400 nm. 100%-skin effects, a substantial increase in transmision was noted. (Solan & Laden,1977).

Route: in vitro. Species: hamster. The effect of test material on transepidermal water loss was evaluated using ventral ear skin obtained from Syrian golden hamsters. A modified flow-through diffusion apparatus was used. Vehicle was water. 25%-positive effects, transepidermal water loss was increased. (Lieb, Nash, Matias & Orentreich,1988).

Route: in vitro. Species: adult human. The hemolytic potential of the test material was measured and expressed as the LD_{50} ie that concentration of test material required to produce 50% lysis of red blood cells. Data for some materials was previously published so only new data has been entered here. 3.7%-calculated LD_{50}. (Reed & Yalkowsky,1987).

Route: in vitro. The sample tested was 99% pure. A model stratum corneum lipid matrix was prepared. To test the effect of glycerol on hydration, samples were made 0, 5, 10 & 15% glycerol by weight with a constant level of 33% H2O. Constant relative humidities (RH) of 6 & 92% were produced using dessicators & a constant temp of 21 degrees C.

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Samples of lipids were spread on microscope slides in uniform layers & then put in humidity chambers. Samples were weighed over a 6 hr period & at 24 & 72 or 96 hr to measure H2O loss or gain. 0 & 10% samples were examined under polarizing light at 6, 24 & 96 hr. 10%, ineffective in preventing H2O loss at 6% RH & liquid crystal character is slowly lost over 96hr; H2O uptake occurred at high RH & at 96hr the glycerol-containing structure is mostly liquid crystal with some being solid. 100%, at low RH, maintained a constant wt over 72 hr; at high RH, steadily took up H2O thruout study & had added its own weight in H2O by 72 hr. (Froebe, Simion, Ohlmeyer, Rhein, Mattai, Cagan & Friberg,1990).

Route: in vitro. Species: rat. No results in computer files. (Peroni, Large & Beylot,1995).

Analytical methodology.. (Ramsey, Lee, Osselton & Moffat,1980b).

(Vaughan,1988).

Blood brain barrier, barrier creams.. Component of barrier cream being tested. (Frosch, Schulze-Dirks, Hoffmann & Axthelm,1993a).

Biological tests other than safety testing and pharmacological tests.. Effects on shrinkage temperaure of goat skin and of canine, bovine and/or human aortae were studied. (Milch,1965).

Radiolabeled test material was used to study lipidogenesis and gluconeogenesis in humans. (Piccardo, Legramante, Papa & Sabella,1967).

Transport of ethylene glycol and glycerol across the dog nephron was studied. (Swanson & Thompson,1969).

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